

VERSION WITH MARKINGS SHOWING CHANGES MADE

1. (Amended) A method of measuring efflux of a chemical [(26)] from a cell [(14, 52, 144, 216, 218)], or a population of cells [(170, 240, 242)] the method including introducing the chemical to the cell and measuring an electrochemical property of a medium [(28, 152, 162, 172)] surrounding the cell with an electrochemical system [(A)] which includes a working electrode [(20, 50, 120, 160, 164, 180, 184, 188, 212, 214, 250)] and a reference electrode [(24, 54)], the property being related to a concentration of the chemical in the medium, the method characterized by:

adding oxygen to the medium to increase a signal strength of the electrochemical property.

3. (Amended) The method of [either one of preceding claims 1 and 2] claim 1, further characterized by:
the cell population comprising a monolayer of cells.

4. (Amended) The method of [either one of preceding claims 1 and 2] claim 1, further characterized by:
the cell being a single cell.

5. (Amended) The method of [any one of preceding claims 1-4] claim 1, further characterized by:
the step of adding oxygen to the medium including bubbling an oxygen-containing gas into the medium.

7. (Amended) The method of [any one of preceding claims 1-6] claim 1, further characterized by:
prior to the step of measuring an electrochemical property of the medium, positioning the cell or population of cells on a substrate [(70, 84, 128, 143, 174, 246)], a surface [(74)] of the substrate having at least one hydrophilic region [(72, 72', 126, 142)] to which at the cell or the population of cells attaches,

the hydrophilic region being surrounded by a hydrophobic region which resists attachment of cells to the surface.

9. (Amended) The method of [either one of preceding claims 7 and 8] claim 7, further characterized by:

the substrate [(70)] including a number of spatially orientated hydrophilic regions [(72', 96)] for spatially orienting a preselected number of cells or groups of cells.

10. (Amended) The method of [any one of preceding claims 7-9] claim 7, further characterized by:

the working electrode being a carbon ring electrode [(50)] , formed on the surface [(74)] of the substrate [(70)].

11. (Amended) The method of [ny one of preceding claims 7-10] claim 7, further characterized by:

the step of introducing the chemical to the cell including injecting the chemical into the cell.

12. (Amended) The method of claim 11, further characterized by:

the step of injecting the chemical into the cell including forming an aperture [(147)] in the substrate and allowing the chemical to diffuse into the cell from an injection tube [(146)] of a diffusional microburette [(140, 204, 224, 226)].

13. (Amended) The method of [any one of preceding claims 1-12] claim 1, further characterized by:

the chemical being a drug used for the treatment of cancer.

14. (Amended) The method of [any one of preceding claims 1-13] claim 1, further characterized by:

the step of measuring an electrochemical property including voltammetric scanning in the region of a cathodic peak of the chemical.

16. (Amended) An apparatus for measuring efflux of a chemical from a biological cell [(14, 52, 144, 216, 218)], or a population of cells [(170, 240, 242)], the apparatus including:

a substrate [(70, 84, 128, 143, 174, 246)] having a surface [(74)] which receives the cell;

a medium [(28, 152, 162, 172)] on the substrate;

an electrochemical monitoring system [(A)] which measures an electrochemical property of the medium surrounding the cell, the property being related to a concentration of the chemical in the medium, the apparatus characterized by:

the substrate surface having at least one attachment region [(72, 72', 126, 142)] to which the cell or population of cells attaches, the region being surrounded by a resistant region [(78)] which resists the attachment of cells.

17. (Amended) The apparatus of claim 16, further characterized by:

a source [(156)] of an oxygen containing gas which supplies oxygen to the medium for increasing the signal strength of the electrochemical property.

19. (Amended) The apparatus of [any one of preceding claims 16-18] claim 16, further characterized by:

the electrochemical system including a carbon electrode [(20, 50, 120, 160, 164, 180, 184, 188, 212, 214, 250)] which is positioned adjacent the at least one attachment region for measuring the electrochemical property of the medium surrounding the cell.

20. (Amended) The apparatus of claim 19, further characterized by the carbon electrode [(50, 160, 164, 180, 184, 188, 212, 214, 250)] defining an annulus which surrounds the at least one attachment region.

21. (Amended) The apparatus of [any one of preceding claims 16-20] claim 16, further characterized by:

the hydrophilic region being sized for attachment of only one cell.

22. (Amended) The apparatus of [any one of preceding claims 16-21] claim 16, further characterized by:

the substrate including a number of spatially orientated hydrophilic regions [(72')] for spatially orienting a preselected number of cells or groups of cells.

23. (Amended) The apparatus of [any one of preceding claims 16-22] claim 16, further characterized by:

a sensor [(122, 124)] formed on the surface of the substrate adjacent the at least one attachment region for detecting at least one of pH, oxygen, and calcium concentration of the medium.

24. (Amended) The apparatus of [any one of preceding claims 16-23] claim 16, wherein the surface includes a plurality of attachment regions [(96)] which each attracts a single cell or a group of cells, each attachment region having an associated working electrode [(88)] positioned adjacent the attachment region.

25. (Amended) The apparatus of [any one of preceding claims 16-24] claim 16, further including a retaining wall [(56)], formed on the substrate [(70)], for retaining the medium around the cell or cells.

26. (Amended) The apparatus of [any one of preceding claims 16-24] claim 16, further characterized by the substrate comprising a mesh, the medium disposed above and below the mesh.

27. (Amended) A method of measuring efflux of a chemical from a biological cell [(14, 52, 144, 216, 218)], or a population of cells [(170, 240, 242)], the method including introducing the chemical to the cell and measuring an property of a medium [(28, 152, 162, 172)] surrounding the cell or population of cells, the property being related to a concentration of the chemical in the medium, the method characterized by:

positioning the cell or population of cells on a surface [(74)] of a substrate by attachment of the cell or the cell population to a region [(72, 72', 126, 142)] of the substrate which permits attachment, the attractive region of the substrate being surrounded by a region [(78)] which resists attachment of cells.

29. (Amended) A method of measuring transport of a chemical [(26)] across a membrane of a human or other biological cell [(14, 52, 144, 216, 218)], the method comprising exposing the cell to the chemical and measuring a property of a liquid medium [(28, 152, 162, 172)] disposed outside the cell, the property being related to a concentration of the chemical in the medium, the method characterized by:

providing a substrate surface [(74)] with a region [(72, 72', 126, 142)] formed from a material to which the cell attaches, the region being surrounded by a portion [(78)] of the surface which resists attachment of a cell;

patterning the substrate using photolithographic techniques to define at least one sensor [(20, 50, 120, 160, 164, 180, 184, 188, 212, 214, 250, 122, 124)] adjacent the attachment region for sensing the property of the liquid medium;

depositing the cell on the region; and

after the step of exposing the cell to the chemical, detecting the property of the liquid medium surrounding the cell and determining the concentration of the chemical in the medium therefrom.

30. (Amended) A method of measuring transport of a chemical across a membrane of a biological cell [(14, 52, 144, 216, 218)], the method comprising exposing the cell to the chemical [(26)], the method characterized by:

providing a substrate surface [(74)] with a site formed from a material to which the cell attaches, the site being surrounded by a portion of the surface which resists attachment of a cell;

depositing the cell on the site;

moving a sensor [(164, 212, 214)] through a wall of the cell to contact the material in the cell; and

measuring a property of a material within the cell with the sensor, the property being related to a concentration of the chemical in the cell and determining the concentration of the chemical in the cell therefrom.